



Yale Institute for Nanoscience  
and Quantum Engineering

**Friday- December 5, 2014**

**12:00 – 1:00 p.m.**

**BECTON SEMINAR ROOM**

**Light lunch to be served at 11:45**

**Dr. Jianping Fu**

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**"Micro/nanoengineering for medicine:  
Examples of stem cell mechanobiology and functional immunophenotyping"**

Synthetic micro/nanoengineered devices and systems are emerging as powerful high-throughput tools for quantitative analysis of cellular functions down to the single-cell level. To approach this exciting opportunity, my group has recently developed a microscale cell culture system composed of geometrically modulated elastomeric poly-(dimethylsiloxane) (PDMS) micropost arrays (PMAs) that can uncouple changes in substrate rigidity from other properties of the substrate (*e.g.* adhesive ligand, adhesion area). Using PMAs, we have studied substrate rigidity as a potent mechanical signal to control stem cell fate. For example, our study has revealed that substrate rigidity can switch differentiation potential of human mesenchymal stem cells (hMSCs) between osteogenic and adipogenic fates. Interestingly, changes in cytoskeleton (CSK) tension can precede differentiation of hMSCs and thus be utilized as a non-destructive predictor for fate decisions of hMSCs at the single-cell level. More recently, we have extended our research to investigate mechanosensitive properties of human pluripotent stem cells (hPSCs) including human embryonic stem cells (hESCs). Our study has provided convincing data suggesting that hPSCs are indeed mechanosensitive and -responsive. Compliant PMAs promote neuroepithelial induction of hPSCs. Furthermore, Pax6+ neuroepithelial cells (NEs) derived from hPSCs on compliant PMAs possess a posterior identity even without any treatment with caudalization factors, and functional specification of motor neurons (MNs) is significantly accelerated and promoted on compliant PMAs. Together, the purity and yield of functional MNs derived from hPSCs within 23 days of culture using compliant PMAs are improved more than 4- and 10-fold, respectively, compared to coverslips or rigid PMAs. Mechanistic study of rigidity-dependent neuroepithelial induction of hPSCs have revealed a multi-targeted mechanotransductive process in hPSCs involving Smad phosphorylation and nucleocytoplasmic shuttling, regulated by rigidity-dependent Hippo/YAP activity and RhoA/ROCK-mediated CSK tension.

I will conclude my talk with our latest effort to leverage highly integrated microfluidics for systems-level functional phenotyping of subpopulations of immune cells isolated directly from unprocessed blood specimens. Our microfluidic immunomonitoring technology will allow rapid, accurate, and multiplexed functional assays on different types or subpopulations of immune cells using a small amount of patient blood, critical for systems-level studies of human immunity and clinical diagnosis of immune disorders and diseases.

**HOST: Paul Fleury / Mark Reed**